A PHASE I/II TRIAL OF INTRAPROSTATIC INJECTION OF CG7870 FOLLOWED BY THREE-DIMENSIONAL CONFORMAL RADIATION THERAPY (3D-CRT) IN PATIENTS WITH CLINICALLY LOCALIZED INTERMEDIATE-RISK PROSTATE CANCER

Nontechnical Abstract

Prostate cancer is the second leading cause of cancer death in men in the United States. The incidence has increased dramatically over the past 25 years, partly because to early detection but also to improvements in tests for a protein substance in the body called prostate-specific antigen (PSA). Normal prostate cells produce PSA but little is released into the bloodstream. In contrast, nearly all prostate cancers produce or release a significantly higher level of PSA. No other cells within vital organs of the body produce PSA. PSA levels increase with increasing age and have been correlated with developing benign prostatic hypertrophy (BHP) and with prostate cancer.

This clinical study is based on a new approach to treatment of prostate cancer in men with disease that has not spread beyond the prostate gland and is at the intermediate stage. The treatment involves injection into of a modified virus into the prostate gland. The virus has been engineered to seek out and kill cancer cells identified by the presence of PSA on their surface. The virus was constructed from a virus similar to the common cold virus, called adenovirus, combined with parts of the human PSA gene. The virus reproduces in the prostate cancer cells (cells containing PSA) and kills them. This virus, called CG7870, affects only a small number of cells that do not contain PSA (10,000:1) so that very few normal cells die. In this study, treatment with CG7870 is combined with a type of radiation called three-dimensional conformal radiation therapy (3D-CRT).

The main goals of the study is to determine that CG7870 is safe when combined with radiation therapy. Other goals are to see if CG7870 is working by testing for PSA at various time points after treatment (weekly from Week 2 through Week 10 after administration of CG7870.)

This study will take place in several centers. The combined enrollment of all centers will be approximately 26 patients with localized cancer of the prostate gland. The study will have two phases. In Phase I, Cohort 1, 2 to 6 patients will receive a single dose of 1×10^{12} (1 trillion particles) CG7870 on the first day of the study. On the fourth day, that is, three days after receiving CG7870, treatment with 3D-CRT will begin. In Phase I, Cohort 2, 2 to 6 patients will receive a treatment in two doses, each of 1×10^{12} (for a total of 2 trillion particles) on Day 1 and Day 22. Treatment with 3D-CRT will begin on Day 4. In Phase II, additional patients will be added for a total of 20 patients to be treated at the highest safe dose determined in Phase I.

Treatment with CG7870 will be administered by injection into the prostate gland using ultrasound guidance, which allows the doctor to see the position of the needle in the prostate on the ultrasound monitor. The ultrasound probe will be placed in the rectum. There will be six injection sites in order to have the virus particles evenly distributed throughout the prostate gland. Prior to this procedure, patients will be given an enema. A local anesthetic

may be given. Patients will be placed on antibiotics to prevent infection. The procedure will take 15 to 30 minutes, and vital signs will be monitored for a minimum of 2 hours afterwards. Blood samples will be take at 30 minutes, 1, 3, 6, and 18 to 24 hours receiving CG7870, and patients will be seen in the clinic daily for 5 days.

Treatment with 3D-CRT will be at the standard dose for patients with intermediate-stage prostate cancer, 180 cGy a day 5 days a week for a total of 41 treatments. During this part of the treatment, patients will be seen weekly for 9 weeks.

Before any study procedures are done, patients will have the study explained to them by the investigator, and they will be able to ask questions. If they decide to enroll in the study, they will be asked to read a written informed consent form, and if they agree to participate, to sign the form. A copy of the signed form will be given to them. For the radiation part of the treatment, there will be a separate consent, including explanation by the radiologist, a chance to ask questions, and reading and signing a consent form. There will also be separate consent forms signed for biopsies and HIV sample collection.

Screening for eligibility will include diagnosis of localized prostate cancer by a biopsy, medical history, physical examination, Eastern Cooperative Oncology Group performance status (evaluation of daily functioning), tumor assessment by computed tomography (CT), magnetic resonance imaging (MRI), chest x-ray, Prostascint (scan after injection of an antibody to help the doctor see the diseased parts of the prostate), and/or other tests as clinically indicated. Laboratory tests will include hematology tests; serum chemistry tests; urinalysis; PSA level and another common test for prostate disease, prostatic acid phosphatase; bleeding function tests; and the test for the human immunodeficiency virus (HIV). During the study other blood and/or urine samples will be collected to test for antibodies to adenovirus, the presence of the experimental drug, CG7870, and tests for other protein substances called cytokines. Each blood sample will be from about 2 to 4 tablespoons.

Patients will be actively involved in the study for approximately 18 months. During the treatment part of the study, patients will be seen daily for 5 consecutive working days after receiving CG7870 then weekly for the next 9 weeks. In the follow-up part of the study, patients will be seen at Months 3, 4, 6, 9, 12, 15, and 18 after receiving CG7870. After completion of the study, patients will be asked to enroll in a separate, long-term follow-up study.

During follow-up visits, at certain time points, some or all of the above tests will be done, and patients will be asked what medications they are taking and whether they have had any adverse events (symptoms or incidents not expected in daily life). In addition, two biopsies will be done during follow-up visits, and other tests may be done as needed.